

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

Claims 1-39 (Cancelled)

40. (Previously presented) The method according to claim 47, wherein said receptor tyrosine kinase is epidermal growth factor receptor (EGFR).

41. (Previously presented) The method according to claim 47, wherein said growth factor precursor is proheparin-epidermal growth factor (proHB-EGF) and said receptor tyrosine kinase is EGFR.

42. (Previously presented) The method according to claim 47, wherein said receptor tyrosine kinase is selected from the group consisting of epidermal growth factor receptor (EGFR), human epidermal growth factor receptor-2 (HER-2), human epidermal growth factor receptor-3 (HER-3), human epidermal growth factor receptor-4 (HER-4), Tumor Necrosis Factor receptor 1 (TNF receptor 1), Tumor Necrosis Factor receptor 2 (TNF receptor 2), tumor necrosis factor receptor superfamily, member 8 (CD 30) and interleukin 6 receptor (IL-6 receptor).

43. (Previously presented) The method according to claim 47, wherein said receptor tyrosine kinase is selected from the group consisting of EGFR and other members of the EGFR family.

44. (Currently amended) A method for ~~identifying~~ testing the ability of a test compound for modulating G-protein mediated signal transduction, comprising contacting a cancer cell containing a receptor tyrosine kinase capable of activation by G-protein mediated signal transduction with a test compound suspected to act on a precursor of a ligand of the receptor tyrosine kinase, and evaluating G-protein mediated receptor tyrosine kinase activation upon exposure of the cancer cell to said test compound as an indication of said test compound's ability to modulate G-protein mediated signal transduction, wherein a lack of G protein mediated receptor tyrosine activation indicates that the ~~thereby identifying a test compound for modulating~~ has the ability to modulate G-protein mediated signal transduction, ~~wherein said cancer cell is selected from the group consisting of pancreatic, prostate, gastric, breast, thyroid, pituitary, adrenal and ovarian tumor cells.~~

45. (Currently amended) A method for modulating growth factor receptor activation by modulating a G-protein mediated signal transduction, comprising:

stimulating G protein mediated signal transduction in a cancer cell having a growth factor receptor tyrosine kinase, wherein the growth factor receptor tyrosine kinase is activated, and wherein said growth factor receptor tyrosine kinase is selected from the group consisting of EGFR and other members of the EGFR family, said cancer cell comprising an extracellular EGFR domain and having a G-protein mediated signal transduction pathway which activates a growth factor receptor, wherein one or more tyrosine residues of the growth factor receptor are

phosphorylated based on the activation of said G-protein mediated signal transduction pathway, the extracellular domain of said receptor is capable of binding to its receptor ligand, and said ligand is generated from a precursor of said ligand by a proteinase-dependent cleavage; and

contacting said cancer cell with a compound which acts on a growth factor precursor in a ~~G-protein mediated extracellular signal pathway which activates a growth factor receptor~~ wherein the growth factor receptor is mediated by its extracellular domain in a G protein mediated signal transduction, and thereby modulating the growth factor receptor tyrosine kinase activation by interrupting G-protein mediated signal transduction, ~~wherein said cancer cell is selected from the group consisting of pancreatic, prostate, gastric, breast, thyroid, pituitary, adrenal and ovarian tumor cells.~~

46. (Canceled)

47. (Currently amended) A method for modulating growth factor receptor activation by modulating G-protein mediated signal transduction comprising:

stimulating G protein mediated signal transduction in a cell having a growth factor receptor tyrosine kinase, wherein the growth factor receptor tyrosine kinase is activated; and

contacting the cell with a compound which directly binds to a growth factor precursor in a ~~G-protein mediated extracellular signal transduction pathway which activates a growth factor receptor~~ wherein the growth factor receptor is mediated by

its extracellular domain in a G protein mediated signal transduction, wherein said G protein mediated ~~extracellular~~ signal transduction ~~pathway~~ includes cleavage of a growth factor precursor, thereby modulating the growth factor receptor tyrosine kinase activation by interrupting G-protein-mediated signal transduction.

48. (Previously presented) The method according to claim 47, wherein said cell is an ovarian cancer cell or a prostate cancer cell.

49. (New) A method for modulating a G protein mediated signal transduction comprising:

providing a cell having epidermal growth factor receptor comprising an extracellular domain and having a G protein mediated signal transduction pathway wherein one or more tyrosine residues on said growth factor receptor are phosphorylated based on the activation of the signal transduction pathway, the extracellular domain of said receptor is capable of binding to its receptor ligand, and said ligand is generated from a precursor of said ligand by a metalloproteinase dependent cleavage;

contacting said cell with a compound capable of activating said signal transduction pathway in the absence and presence of an inhibitor of said metalloproteinase dependent cleavage;

measuring tyrosine phosphorylation of said receptor in said cell to determine whether said signal transduction pathway has been activated;

comparing the level of tyrosine phosphorylation of said receptor in said cell in the absence and presence of said inhibitor wherein a reduction in the level of tyrosine phosphorylation of said receptor in the presence of said inhibitor indicates that releasing said receptor ligand from said precursor is critical for activation of said signal transduction pathway in said cell and said activation is dependent on the interaction between the extracellular domain of said receptor and its receptor ligand.